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## If We Diagnose Herpes Zoster, Should We Search for Any Underlying Malignancy?

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### Abstract

Whether the risk of cancer is increased among patients with herpes zoster (HZ) is unclear. If we diagnose herpes zoster diagnosis, should we search for any underlying malignancy? Is there any relationship between herpes zoster and a malignancy such as breast cancer? A 34-year-old woman with a history of herpes zoster presented to the emergency room with chest pain because of postherpetic neuralgia. Thoracic CT images revealed metastatic lesions in the window of the lung parenchyma. An irregular tumoral mass of the left breast and pathologic lymph nodes at the left axillary fossa were detected. Patient diagnosis was confirmed with breast ultrasonography (usg) and breast mammography examinations. Patients who had one of the 14 underlying diseases, i.e. brain tumor, lung cancer, breast cancer, esophageal cancer, gastric cancer, colorectal cancer, gynecologic cancer, malignant lymphoma, systemic lupus erythematosus, rheumatoid arthritis, diabetes mellitus, hypertension, renal failure, and disk hernia, displayed a 1.8–8.4-fold increased risk of HZ events compared to patients with none of these diseases. A review of the literature revealed studies documenting an association between the diagnosis of herpes zoster and a subsequent diagnosis of malignancy.

**Keywords:** postherpetic neuralgia; advanced breast cancer.

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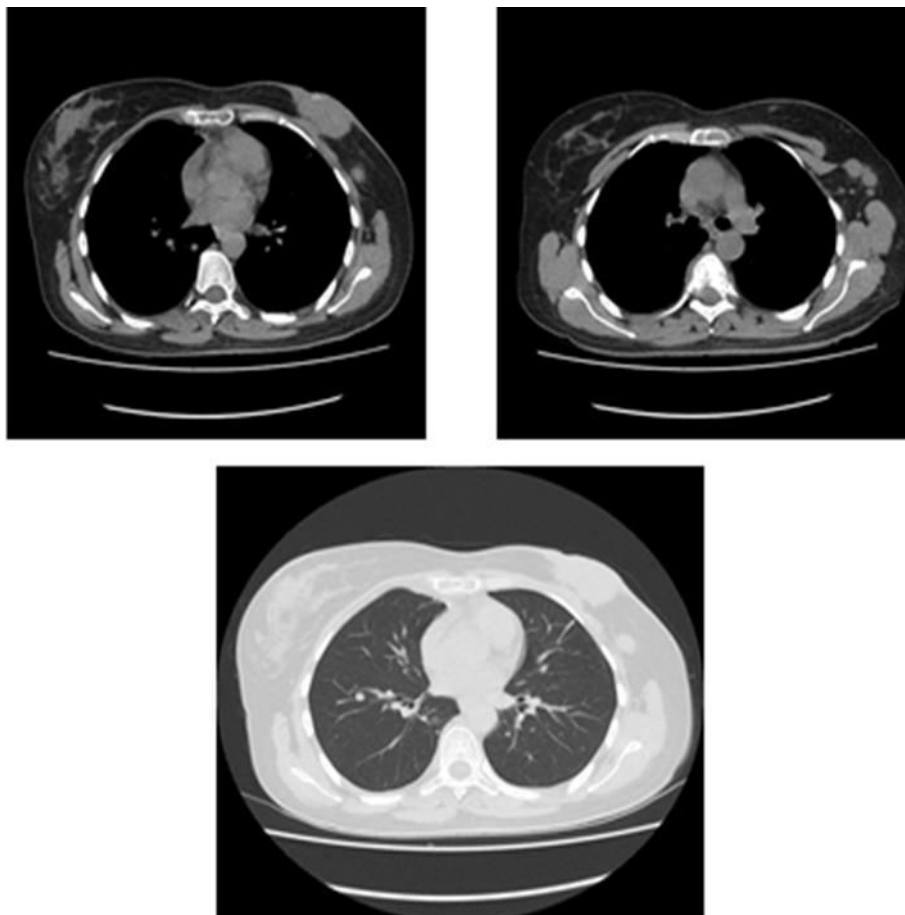
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## 1. Introduction

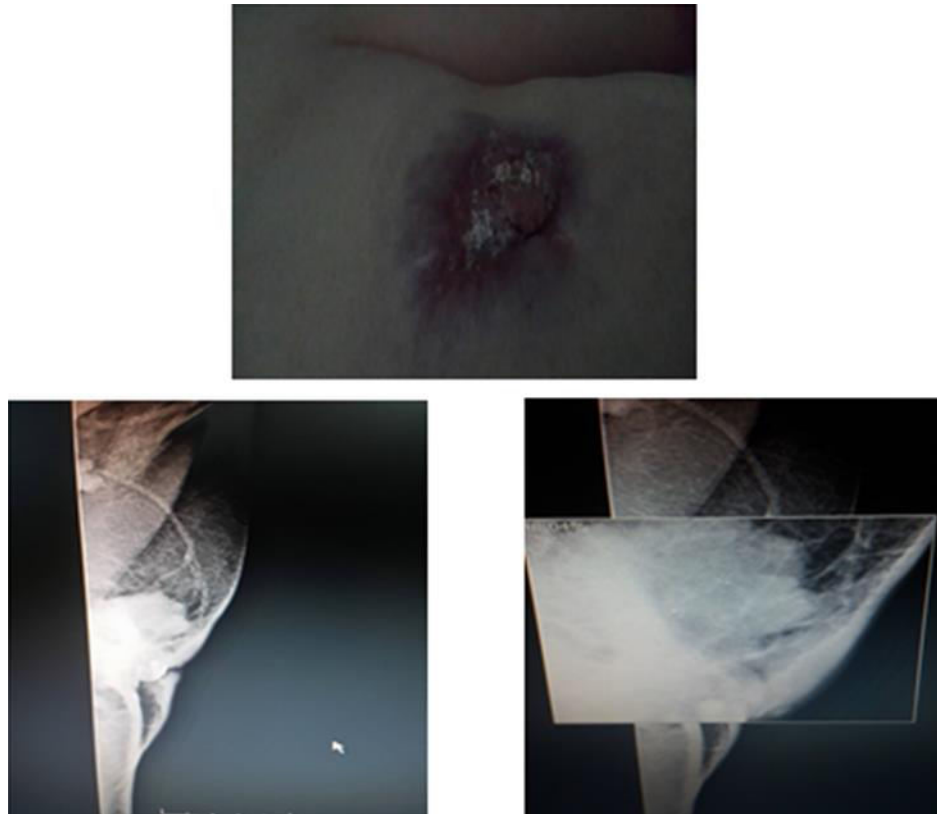
Whether the risk of cancer is increased among patients with herpes zoster is unclear. If we diagnose herpes zoster diagnosis, should we search for any underlying malignancy? Is there a relationship between herpes zoster and malignancy such as breast cancer ?

## 2. Case Report

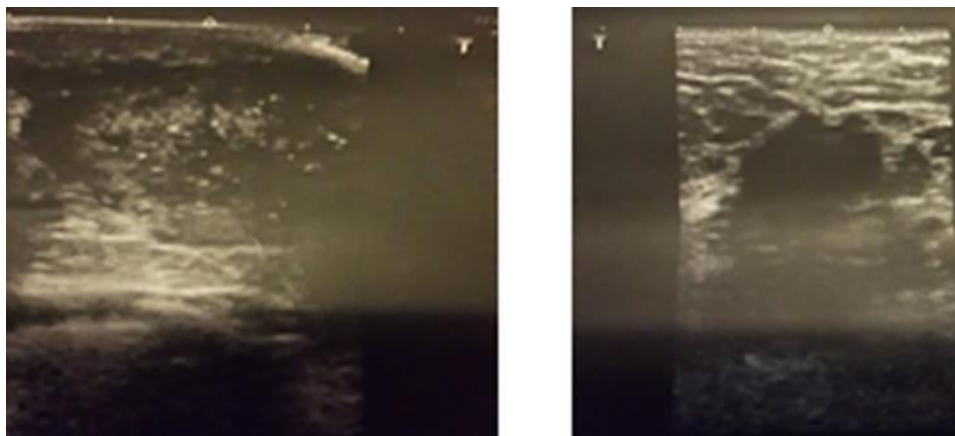
A 34-year-old woman with a history of herpes zoster presented to the emergency room with chest pain because of postherpetic neuralgia. In order not to miss other chest pathologies, a chest CT scan was performed. Thoracic CT images revealed metastatic lesions in the lung parenchyma. In addition, when we looked to the chest wall and soft tissues we found that left breast volume was decreased when compared with the right. An irregular tumoral mass lesion on the retromammary area of the left breast and pathologic lymph nodes at the left axillary fossa were detected (Figure 1 and Figure 2 and Figure 3). Patient diagnosis was confirmed with mammography examinations and breast usg (Figure 4, Figure 5, Figure 6, Figure 7 and Figure 8).



**Figure 1, Figure 2, Figure 3:** Thoracic CT images revealed tumoral mass lesion on retromammary area of the left breast, pathologic lymph nodes at the left axillary fossa and metastatic lesions



**Figure 4, Figure 5, Figure 6 :** The mass was fixed to the skin and underlying chest wall. The patient had nipple retraction and mammogram revealed a mass in the subareolar region .



**Figure 7, Figure 8:** Ultrasound revealed a complex mass. The mass was suspicious for malignancy (Breast Imaging Reporting and Data System Category 4)

### 3. Discussion

Herpes zoster, also known as shingles, is typically characterized by a painful, blistering dermatomal rash. The estimated lifetime risk of HZ in the general population is approximately 30%, with the risk increasing sharply after 50 years of age [1]. Hope-Simpson showed that HZ results from reactivation of the varicella-zoster virus in the sensory ganglia after a long latency period following primary infection from varicella [2]. In some

patients, particularly in the elderly, the pain continues to persist after the rash heals and develops into postherpetic neuralgia (PHN), which is the most common complication. This causes physical disability, emotional distress and interference with daily activities and sleep.

The reactivation of latent infection results from declining specific cell-mediated immunity, which subsequently engenders HZ [3]. The incidence of HZ per 1,000 person-years ranges between 1 and 5 [4]. Associations between the incidence of HZ and malignancies such as lymphoma, human immunodeficiency virus (HIV) disease, cancer, autoimmune disease, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and psychological disease have been recognized [5,6,7].

Patients who had one of the 14 underlying diseases, i.e. brain tumor, lung cancer, breast cancer, esophageal cancer, gastric cancer, colorectal cancer, gynecologic cancer, malignant lymphoma, SLE, RA, DM, hypertension, renal failure, and disk hernia, displayed a 1.8–8.4-fold increased risk of HZ events compared to patients with none of these diseases [8].

A review of the literature revealed several studies documenting an association between diagnosis of herpes zoster and subsequent diagnosis of malignancy.

Iglar K. et al. showed that the increase in adjusted cancer risk following a herpes zoster diagnosis was 19% within the first 180 days after diagnosis and 11% at 1 year [9].

Sørensen et al. compared the incidence of malignancy among patients admitted to hospital with herpes zoster with the expected rate of malignancy. The relative risk was reported as 1.2, with the risk being substantially elevated during the first year of follow-up and especially for hematological cancers, specifically, non-Hodgkin's lymphoma, multiple myeloma, and leukemia [10].

Buntinx et al. conducted a retrospective cohort study using a patient registry of 37 general practices in Belgium and found a statistically significant increase in cancer risk following a diagnosis of herpes zoster in all patients over the age of 65. When the data were stratified by sex, the increase was significant only for women [11].

S J Cotton et al. conducted the largest study, and were the first to show a clear association between zoster and a subsequent diagnosis of cancer. Following analysis of the primary care records of 13,248 patients with a diagnosis of zoster, this study shows that the risk of a cancer diagnosis in adults is significantly increased. The magnitude of the risk varied between cancers, and was highest in younger patients. The median time from zoster to cancer was over 2 years. There were proportionally more cancers in the patients with a history of zoster compared with those without zoster for all age groups and both male and female patients. This was more marked in the first 90 days following diagnosis and in patients over the age of 65 years [12].

Hui-Fen Chiu et al. found that HZ patients were 1.58 times as likely as the general population to develop subsequent cancer during a 1-year follow-up period, after controlling for potential confounders [13].

With these reports the mechanisms that might explain the increased risk of subsequent malignancy in patients

with HZ are unclear. Before diagnosis, cancers are often present in a preclinical or undetectable form. Thus, HZ could be an early manifestation of immune impairment associated with malignancy [11]. An alternative hypothesis is that the reactivation of varicella zoster virus triggers immunologic mechanisms, such as tissue antigen alteration or antigenic stimulation, which could result in cancer [11]. Reports that malignancies had developed at the sites of previous HZ infection are consistent with this hypothesis. Finally, cell-mediated immunity has an important role in the reactivation of VZV and the maintenance of immunologic surveillance control of malignancy. A disorder in host immunity could lead to both HZ and malignancy, either of which may appear first.

#### **4. Conclusion**

An association of zoster with a prior diagnosis of cancer strongly suggests that the immune system is a determinant factor that may link zoster with cancer. Various mechanisms have been suggested for this: There may be a reduction in cell-mediated immunity, allowing zoster to manifest itself and a concurrent reduction in immune surveillance for cancer; zoster may be an early manifestation of an impaired immune system caused by occult cancer; and the zoster virus may provoke an immunological mechanism that weakens immune surveillance for cancer cells allowing tumor escape, or directly causing cancer [11,14,15].

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